REMARKS:

In the Office Action dated January 9, 2009, claims 6, 7, 10, 11 and 14-17, in the above-identified U.S. patent application were rejected. Reconsideration of the rejections is respectfully requested in view of the above amendments and the following remarks. Claims 6, 7, 10, 11, and 14-15 remain in this application, claims 1-5 and 16-17 have been canceled, claims 8, 9, 12 and 13 have been withdrawn, and new claims 18-22 have been added to the application.

Claims 11 and 15 were rejected under 35 USC §102(e) as anticipated by Celeste (USP 5,658,882) as evidenced by Yamashita. The office action acknowledges that angiogenesis is supported in the priority document but contends that the term "matrix" is not supported by the priority document. Applicants respectfully point out that a matrix is a specific type of carrier and carriers are clearly disclosed in the priority documents. A matrix is a typical carrier for BMP proteins and bone matrix is a natural carrier of BMP-proteins. The term "carrier" is widely interpreted as a "means of transmitting active substance: a neutral substance to which an active ingredient or agent is added as a way of applying or transferring the ingredient or agent". One skilled in the art would know that a matrix can be used as a carrier for BMP proteins as shown by Ripamonti (1993) (copy enclosed). Ripamonti describes different carrier systems for BMPs as a summary of experimental studies in primates (monkeys), e.g. on page 14, 1st column, bottom: "The aim of this paper is to present a concise review of BMPs, and to focus selectively on different classes of carriers and substrata as delivery systems for them." On page 16, 1st column it reads: "Thus, a carrier substratum is required for

optimal delivery of osteogenic activity initiated by BMPs bound to the surface of the carrier. The restoration of biological activity after dissociative extraction and reconstitution of BMPs with insoluble collagenous matrix indicates that components of the extracellular matrix of bone act as carriers for the functional expression of BMPs (53). .... Previous studies have shown that the insoluble collagenous carrier provides an optimal substratum for recruitment and anchorage of progenitor cells, and subsequent proliferation and differentiation into osteoblasts (27,32,34). The importance of collagenous matrix in development and regeneration has been extensively demonstrated (35)." Ripamonti clearly indicates that a collagen matrix can be regarded as a carrier and that the terms "collagenous matrix" and "collagenous carrier" have the same meaning. As can be gathered from Ripamonti, carriers without a collagenous matrix as e.g. hydroxyapatite are also a possibility for the release of BMPs. Toriumi et al. (1991) (copy enclosed) shows that among experts, a bone matrix was considered to be a "carrier". Toriumi describes a test for the detection of osteoinductivity of recombinant BMP-2 in large defects (3 cm) in the jawbone of dogs. As "carrier" for BMP-2, bone matrix is used (page 1102, first column under "SUBJECTS AND METHODS": "The carrier material used in this study was demineralized dog bone powder matrix ...".) Inactivated bone matrix was initially the mostly commonly used carrier for BMPs since the bone matrix is a natural carrier of BMPs. Both Ripamonti and Toriumi show that among experts a matrix is regarded as a carrier for BMP. Thus a skilled artisan automatically considered the term "matrix" as being implied when reading the term "carrier" since

for many materials both the term "carrier" and the term "matrix" is correct and commonly used. A matrix for BMPs, as e.g. the bone matrix, can be considered to be the carrier. A carrier, however, is not always a matrix since matrix-free carriers exist, e.g. gels. "Carrier" is thus the broader term which also comprises a matrix. In view of the definitions commonly used in the art, new claims 20 and 21, which do not specifically recite the term "matrix", would still encompass a matrix due to the term "carrier". Claims 11 and 15 have been amended to clarify that the matrix is a carrier. Applicants contend that claims 11 and 15 are supported by the disclosure regarding carriers in the priority document filed on August 10, 1993 and request that this rejection be withdrawn.

Claims 10, 11, and 14-17 were rejected under 35 USC §112, first paragraph, as lacking enablement for a biologically functional part of SEQ ID NO:2 where the biologically functional part has tissue inductive capability or mitogenic capability. The office action acknowledges that the present application is enabling for a biologically functional part which has osteoinductive capability. Though applicants respectfully disagree with this rejection, the claims have been amended to recite "osteoinductive capability" in order to advance the examination of the application. In view of the above amendments, applicants request that this rejection be withdrawn.

Claims 6 and 7 were rejected under 35 USC §112, first paragraph, as lacking enablement regarding the treatment and regeneration of teeth. The office action points out a Wikipedia excerpt which indicates that no known method exists in order to regenerate large amounts of tooth structure (no indication is given for what a large

amount might be). Applicants point out that in the passage cited by the office action (under "Restorations") only materials (glass ionomer, amalgam, gold, porcelain etc.), which are currently used in dental surgery, are listed. Wikipedia does not discuss future possibilities for treating teeth. Wikipedia entries can be created and edited by anyone and thus may not accurately reflect the knowledge of experts in particular fields. For example, a family dentist is unlikely to know about treatments and products which are not yet approved by the FDA but could create a Wikipedia entry regarding dental restorations. Despite the cited Wikipedia entry, it is known in the art that cytokines can be used for the regeneration of dentin and thus for the treatment of teeth. MP52 belongs to the TGF-β superfamily, and has a close relationship to the BMP-proteins. Such cytokines are known to be useful for the regeneration of dentin. Applicants point out the post-published document WO 96/26737 which describes applications of morphogens to which BMPs belong. Under "Summary" WO 96/26737 reads:

> "It is an object of this invention to provide means for inhibiting loss of dental tissue in mammals, as well as means for inducing regeneration thereof. It is an object of the present invention to provide means for stimulating proliferation and differentiation of odontoblasts in mammals, particularly primates. It also is an object of the present invention to provide means for stimulating expression of the odontoblast phenotype, including production of mineralized dentine matrix, by mammalian tooth pulp tissue, including primate tooth pulp tissue such as human tooth pulp tissue."

In particular, see Example 1, wherein it is shown that dentin formation is induced by OP-1, which is also known as BMP-7. A comparable result is also

shown in the post-published article of Nakashima (J. Dent. Res. 73(9): 1515-1522, (1994), copy enclosed) by using BMP-2 and BMP-4. On page 1520 at the end of the article it reads: "The present study demonstrated the utility of recombinant human BMP-2 and BMP-4 as bio-active pulp-capping agents. These morphogenetic factors can induce a large amount of dentin on amputated pulp without affecting the remaining pulp." Thus, applicants contend that dentin can be regenerated with suitable cytokines such as MP52 and thus the present application does enable a method for treating damage to teeth and for regenerating teeth. In view of these amendments, applicants request that this rejection be withdrawn.

Claims 6, 7, 10, 11 and 14-17 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as unpatentable over claims 18, 19, 22-24, 26 and 27 of co-pending application no. 11/545,480 in view of Yamashita. Since both of these applications are currently pending, the claims may change before one of the applications is allowed. In view of this, applicants intend to file a terminal disclaimer when it is clear what claims will be allowed in these applications and that the allowed claims are obvious over the claims in the co-pending application.

In the event this paper is not considered to be timely filed, the Applicant respectfully petitions for an appropriate extension of time. Any fee for such an extension together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account No. 02-2135.

Respectfully submitted,

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